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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,421	10/16/2003	Wei Han	PH 7474 NP	7985

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LOUIS J. WILLE
BRISTOL-MYERS SQUIBB COMPANY
PATENT DEPARTMENT
P O BOX 4000
PRINCETON, NJ 08543-4000

EXAMINER

TRUONG, TAMTHOM NGO

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 10/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/687,421

Applicant(s)

HAN ET AL.

Examiner

Tamthom N. Truong

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2006.
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-7 and 9-21 is/are pending in the application.
4a) Of the above claim(s) 9-13 is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-7 and 14-21 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

Applicants' amendment of 6-12-06 has been fully considered. The amended claims and applicants' argument have overcome the previous rejections of 112/2nd paragraph (items b-e), and 103 based on **Sadhu et. al.** (US'277). However, the amendment has not overcome the previous rejections of 112/2nd (item a) and 112/1st paragraph. Also, amended claims raise the following new ground of rejections.

Applicants' traverse on the restriction is well taken. However, it is maintained that the original formula I is an improper Markush group for reasons stated in the previous action. The reference of Sadhu et. al. was cited to show that quinazolinone compounds **can have different effects**, and thus, a restriction was proper and made FINAL.

Claims 14-21 have been added, and are drawn to pharmaceutical composition of formula I.

Claims 9-13 remain withdrawn from consideration as being drawn to the non-elected subject matter.

Claims 1-7 and 14-21 are considered herein.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Scope of Enablement:** Claims 1-7 and 14-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the make and use of compounds of formula I wherein G is *pyridyl or phenyl* while A-B is a *biphenyl* or *methoxy-phenyl*, does not reasonably provide enablement for the make and use of compounds of formula I wherein G is another ring while A-B is a *phenyl group substituted with a heterocycle*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The breadth of the claims;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;
- (6) The quantity of experimentation necessary;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 1 recites a formula I of a quinazolinone substituted with G, A-B, R^{4b}. The substituent of A-B represents countless combinations of ring or ring systems (A, B or Y) and

divalent groups represented by X. The substituent of G represents a myriad number of rings for ring systems represented by formula IIa defined for G. The ring (formula IIa) defined for G has substituent R, two of which could form a ring fused to either ring D or E (of formula IIa). Thus, G could also represent a tricyclic or tetracyclic system. Each of the group defined for G, A, B are substituted with R, R⁴, R^{4a} that are further substituted with other variables (e.g., R², R^{2a}, R³, R⁶-R⁹ etc.) which in turn represent several functional groups, rings or ring systems. Thus, the claimed formula I represents an extraordinary number of compounds, and not just substituted quinazolinone. Claims 2-6 depend on claim 1, and still recite an extensive number of rings and functional groups. Claim 7 depends on claim 1, and recites species wherein P₄ is another ring while M₄ is a *phenyl substituted with a heterocycle*. Claims 14-21 depend on claims 1-8, and carry out the same broad scope.

The amount of direction or guidance presented:

The generic scheme diagramed in Schemes 1-5 only provide guidance for the skilled chemist to make a quinazolinone compound having P₄ as a phenyl group, and M₄ also as a phenyl group. Examples 1 and 2 describe the process of making quinazolinone compound with G as a pyridinyl group, and A-B as a biphenyl or methoxyphenyl group. The specification does not teach how other compounds of formula I can be made even in a generic way, nor does it provide examples for species with M₄ as a *phenyl group substituted with a heterocycle* (recited in claim 7). Although the specification provides dosages for the claimed compound, there is no evidence if any compound of formula I has any biological activity. Thus, the specification fails to provide sufficient enablement for the large Markush group of formula I recited in claims 1-7.

The state of the prior art:

By the teaching of Sadhu et. al. (US 6,518,277 B1), the skilled chemist could obtain guidance for making and using compounds of quinazolinone substituted with phenyl or pyridyl at the 3rd position (or corresponding to G), and $-\text{CH}_2\text{-S-}$ (substituted purine) at the 2nd position (or corresponding to the original Z-A-B). However, the teaching of Sadhu et. al. would not sufficiently guide the skilled chemist to make other compounds of the claimed formula I, or many species in the instant claim 7. Thus, the state of the prior art cannot remedy the deficiency in the enablement provided by the instant disclosure.

The relative skill of those in the art:

Even with the advanced training, the skilled clinician would have to carry out extensive research to make and select an effective compound from the large Markush group of formula I. Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50} , therapeutic index and pharmacokinetic profile for each compound. Given a large Markush group of the claimed formula I, such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary:

The pharmaceutical art has always been unpredictable. Compounds of different rings or ring systems do not always share the same physical, chemical or biological activity. Note, even the same quinazolinone core disclosed by Sadhu et. al. has different biological activity from those of the claimed formula I. Thus, there is no logical rational to expect compounds of

different cores in the claimed formula I to possess the same biological activity. With the limited teaching provided by the instant disclosure and state of the prior art, the skilled chemist would have to engage in undue experimentation to make and use compounds of formula I.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-6, 14-19 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. In claim 1, the limitation of “*alternatively, when 2 R groups are attached to adjacent atoms, they combine to form methylenedioxy or ethylenedioxy;*” which has indefinite metes and bounds because it is unclear if these R groups forming a ring fused with ring D, ring E or both. Thus, it is unclear if group G could be a bicyclic, tricyclic or tetracyclic system. Applicants argued that there could only be 4 options to the limitation of 2 R groups fused with D and E, and thus, it is not indefinite. However, as implicated by formula IIa, G appears as a bicyclic system when in fact, G could be monocyclic, bicyclic, tricyclic, tetracyclic. It could also be ortho-fused or peri-fused. This raises the ambiguity in the definition of G, and thus, indefiniteness.

Art Unit: 1624

- b. The proviso in the definition of B is extraneous because it includes variable Z which has been deleted.
- c. Claim 21 is an improper dependent claim because it depends on claim 8 which has been cancelled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 3. Claims 1, 2, 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by **Pandit et. al.** (CA 79:115526). The chemical abstract discloses the compound of “4(3H)-*Quinazolinone, 3-phenyl-2-(2-phenyl-5-pyrimidinyl)-*” which reads on the instant formula I with the following substituents:

- i. G is formula IIa wherein D is absent, and E is a phenyl group substituted with R (as hydrogen);
- ii. A is pyrimidyl;
- iii. B is Y which is a phenyl group;
- iv. R^{4b} is hydrogen.

No pending claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

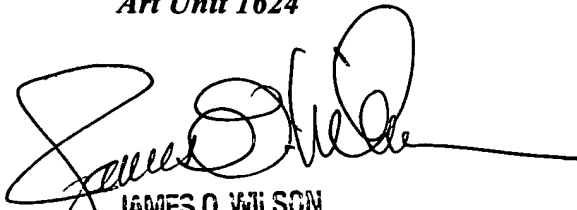


Tamthom N. Truong

Examiner

Art Unit 1624

9-28-06



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600